REMARKS

I. Status of the Claims

Claims 1-28 were initially filed. As the result of a restriction requirement, claims 17-28 have been withdrawn from consideration. Upon entry of the present amendment, claims 1-16 are pending under examination and claims 17-28 are canceled without prejudice to future revival.

II. Amendments to the Specification

The abstract is amended to correct a typographic error. No new matter is added.

III. Claim Rejections

A. 35 U.S.C. §112, First Paragraph

Claims 1-16 were rejected under 35 U.S.C. §112, first paragraph, for alleged inadequate written description. Applicants respectfully traverse the rejection.

The written description requirement requires the claimed subject matter to be described in the specification in such a manner as to reasonably convey to one of skill in the art that the inventors, at the time this application was filed, had possession of the claimed invention. The Examiner alleged that the specification failed to provide a written description of a method by which an exon of any eukaryotic genomic fragment can be identified and mapped to a genomic location. Specifically, the Examiner alleged that the specification failed to teach how to determine the proper size of genomic fragments to be included in a phage display library, other than in the example of H11 P1. Citing the Jacobsson articles in *Biotechniques*, the Examiner further asserted that the tertiary structure of a protein, such as a second binding motif or a second polypeptide chain involved in the interaction with the binding partner, may prevent identification of some exons using the claimed method. Applicants respectfully disagree with the Examiner on these points.

First of all, the specification provides sufficient guidance for a person of skill in the relevant art to determine the appropriate size of subsequences in a phage display library. Such guidance is provided both as general discussions and as examples with specific factors to

consider. For instance, the specification teaches that the appropriate size of the subsequences inserted into a phage display library can be determined based on the relative numbers of introns and exons, and that the appropriate size of the subsequences should ensure the library to have enough members to represent all or the vast majority of the genomic fragments to be analyzed (page 13, lines 25-31). Further discussions on the size restrictions relating to the gene structure, such as intron-exon pattern, size of the target region, stop codon frequency, exon size, *etc.*, can be found, *e.g.*, on page 14, line 12, to page 15, line 5. Moreover, the specification teaches how to determine the appropriate size of the subsequences by way of example. In Example 1 on page 30 and in Figure 1, the process of insert size selection for H11 P1 is described, which takes into consideration factors such as exon size, stop codon frequency, and resulting library size. Because the specification offers both generalized description and specific examples on how to choose the proper size of subsequences to be inserted into a phage display library, one of skill in the art would, upon reading this specification, that the inventors had the claimed invention in their possession at the time this application was filed.

Secondly, the Examiner's assertion that the claimed method may not successfully identify every exon in a eukaryotic genomic fragment is irrelevant to the written description assessment. As discussed above, the written description requirement only requires that the claimed invention be sufficiently described. On the other hand, whether or not a claimed invention is operable could be relevant to the enablement assessment. Although the Examiner did not raise an enablement rejection, Applicants contend that even the enablement requirement does not require the claimed method to be operable for identifying every exon in a eukaryotic genomic fragment. The enablement requirement requires the specification to describe the claimed invention so as to allow one of skill in the art to make and use the invention. MPEP §2164. As stated in MPEP §2164.01(b), "[a]s long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. §112 is satisfied." Applicants contend, and the Examiner appeared to agree, that the present specification describes a method that would allow the identification of at least some, if not most, exons from eukaryotic

genomic fragments, which clearly bears a reasonable correlation to the entire scope of the claim. Thus, even if the Examiner is correct in that the claimed method may not be used to identify every exon in a eukaryotic genome, this factor alone is insufficient to support a written description or enablement rejection.

In summary, the Examiner has not shown that the claimed invention is not adequately described in the specification. Accordingly, Applicants respectfully request the withdrawal of the written description rejection.

B. 35 U.S.C. §102

Claims 1-3, 8, 9, 13, 14, and 16 were rejected under 35 U.S.C. §102(b) for alleged anticipation by Fack *et al.* Applicants respectfully traverse the rejection.

To anticipate a pending claim, a prior art reference must provide, either explicitly or implicitly, all limitations of the claim. MPEP §2131.

The pending claims are drawn to a method for identifying an exon in a eukaryotic genomic fragment. The method comprises the following steps: first, expressing a population of subsequences of the genomic fragment in a phage display library, ***wherein the population comprises protein-encoding subsequences and noncoding subsequences***; second, screening the phage display library with a binding partner to identify an expressed subsequence that specifically binds to the binding partner; and third, mapping the expressed subsequence to the physical location in the genomic fragment, thereby identifying the exon.

The Fack *et al.* reference describes a method for identifying antibody epitope using a gene-fragment phage display library, which expresses fragments of the coding sequence for a protein of interest (see, *e.g.*, page 46, left column, section 3.1, "[w]e constructed a gene-fragment phage display library using the 3.6 kb insert of pUCHTN-M containing the coding sequence of the Hantaan virus M-fragment digested with *DNase* I and cloned in fUSE5 with FUS-P linkers." Emphasis added). In other words, Fack *et al.* used a phage display library that expressed only fragments of the coding sequence of a protein; the library did not include any "***noncoding subsequences***." Neither is the inclusion of "noncoding sequences" suggested

anywhere in the reference. The Fack *et al.* reference therefore does not provide all claim limitations and cannot anticipate the pending claims.

As such, Applicants respectfully request the withdrawal of the anticipation rejection.

C. 35 U.S.C. §103

Claims 1-4 and 8-16 were rejected under 35 U.S.C. §103(a) for alleged obviousness over Fack *et al.* in view of Buckler *et al.*, and claims 5-7 were rejected further in view of Winter *et al.* Applicants respectfully traverse the rejection.

To establish a *prima facie* case of obviousness, three basic criteria must be met: first, the prior art references must teach or suggest all the claim limitations; second, there must be some suggestion or motivation, either in the references or in the knowledge generally available to one of ordinary skill in the art, to combine the limitations; third, there must be a reasonable expectation of success in combining the limitations. MPEP §2143.

As discussed above, Fack *et al.* did not teach or suggest at least one limitation of the pending claims: the limitation of "noncoding subsequences." On the other hand, WO92/13071 relates to a method for exon amplification, and the Winter *et al.* reference relates to recombinantly producing antibodies using phage display technology. Neither supplies, explicitly or implicitly, the missing claim limitation of "noncoding subsequences." Thus, not all claim limitations are provided by the cited references.

Because no *prima facie* obviousness is established, the withdrawal of obviousness rejection is respectfully requested.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

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